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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/986,186	12/05/97	PETERSON T	8757-009

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EXAMINER	
BRUSCA,J	
ART UNIT	**PAPER NUMBER**
1636	14

DATE MAILED: 07/14/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/986,186	Applicant(s) Peterson et al.
	Examiner John S. Brusca	Group Art Unit 1636

☒ Responsive to communication(s) filed on *6/2/99*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *27-42* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *27-42* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 6/2/99 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/986186 is acceptable and a CPA has been established. An action on the CPA follows.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons:

Nucleic acid sequences appear on pages 85, 86, and 104 and in the Brief Description of the Drawings of Figures 5A-5G, 6C, and 10 but applicants have not submitted a Sequence Listing as set forth in 37 CFR § 1.821 (see MPEP § 2422).

Applicants are required to comply with all of the requirements of 37 CFR § 1.821 through 1.825. Any response to this office action which fails to meet all of these requirements will be considered non-responsive. The Applicant's attention is directed to the attached Notice to Comply with the Sequence Rules. The nature of the sequences disclosed in the instant application has allowed an examination on the merits, the results of which are communicated below.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 29, 30, and 33-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification describes a method of making a biased combinatorial gene expression library comprising DNA fragments isolated from a plurality of species of organisms in which the selection is by hybridization to nucleic acid probes. The described probes listed on pages 63-64 are polyketide biosynthetic loci probes, actinorhodin biosynthesis (actI) probes, spore pigment biosynthesis (whiE and eryA1) probes, antibiotic or secondary metabolism biosynthetic loci probes, peptide synthetase gene probes; thiostrepton, virginiamycin,

valinomycin, and actinomycin biosynthetic loci probes; peptide synthase probes, and aminoglycoside synthase probes. The specification does not provide written support for probes of biosynthetic genes for: mevalonic acid, glucose transfer systems, beta lactams, macrolides, alkaloids, bryostatins, carotenoids, steroids, retinoids, tetracycline, oxytetracycline, puromycin, doxyrubicin, taxol, chloramphenicol, nalidixic acid, mithramycin, novobiocin, vulpinic acid, usinic acid, kainic acid, podophyllotoxin, brevitoxin, camptothecin, or artemisinin.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 27-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 27-42 are indefinite for recitation of the phrase "each expression construct containing cDNA or genomic DNA fragments some of which are preselected from a plurality of species of donor organisms" because it is not clear whether all constructs are selected from a pool of expression constructs obtained from a plurality of species of donor organisms. The phrase is further indefinite because it is not clear how fragments can be selected from organisms since DNA fragments are not organisms. The rejection would be overcome by amending claims 27 and 28 to recite "wherein each expression construct comprises cDNA or

genomic DNA fragments obtained from a plurality of species of donor organisms and each expression construct has been selected."

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (f) he did not himself invent the subject matter sought to be patented.

9. Claims 27-32, and 35-42 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The instant claims are drawn to gene expression libraries comprising constructs comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms, in which the constructs have been selected for sequences that encode proteins that are involved in secondary metabolism. In some embodiments the donor organism is from an environmental sample from soil, deposits near hot springs or thermal vents, freshwater or seawater filtrates, or marine or estuarine sediments. In some embodiments the library is in a host cell. In some embodiments the selection is performed by hybridization to a secondary metabolism gene. In some embodiments the secondary metabolism gene is involved in antibiotic synthesis; thiostrepton, virginiamycin, valinomycin, or actinomycin synthesis.

U.S. Patent No. 5,824,485 shows throughout a gene expression library comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms, in which the constructs have been selected for a specific property and the constructs are operably linked to elements that allow for expression in a host cell. Columns 13-14 provide guidance to isolate donor organisms from an environmental sample from soil, deposits near hot springs or thermal vents, freshwater or seawater filtrates, or marine or estuarine sediments. Columns 31 and 32 provide guidance to make selected libraries that encode proteins that are involved in secondary metabolism, such as genes involved in the synthesis of antibiotic synthesis; thiostrepton, virginiamycin, valinomycin, or actinomycin synthesis.

Therefore U.S. Patent No. 5,824,485 anticipates the claimed invention. U.S. Patent No. 5,824,485 has a different inventive entity than the instant application.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 27, 28, 41, and 42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21 and 22 of U.S. Patent No. 5,783,431 in view of Vining.

The instant claims are drawn to gene expression libraries comprising constructs comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms, in which the constructs have been selected for sequences that encode proteins that are involved in secondary metabolism. In some embodiments the selection is by hybridization to secondary metabolism genes, and the library is in a host cell.

Claims 21 and 22 of U.S. Patent No. 5,783,431 are drawn to a method of making a gene expression library comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms, in which the constructs have been selected for a specific property and the constructs are operably linked to elements that express the sequence in a host cell. Claim 22 is drawn to the method of claim 21 in which the selection is by hybridization to a metabolic pathway gene. Claims 21 and 22 of U.S. Patent No. 5,783,431 are not drawn to libraries selected for sequences that encode proteins that are involved in secondary metabolism.

Vining shows in the abstract that secondary metabolism genes are preferably isolated from genomes of different organisms because they are of ancient origin and are better

conserved between species of organisms than within related genes of the same organism. Vining shows throughout many examples of secondary metabolism genes and that secondary metabolites are useful as antibiotics, mycotoxins, insecticides, and herbicides.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the method of library construction of claims 21 and 22 of U.S. Patent No. 5,783,431 by selection for sequences that encode proteins involved in secondary metabolism because Vining shows that secondary metabolism genes are best obtained from different species of organisms and are useful to make antibiotics, mycotoxins, insecticides, and herbicides.

12. Claims 27, 37, and 41 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3, 8, and 10 of U.S. Patent No. 5,824,485 in view of Vining.

The instant claims are drawn to gene expression libraries comprising constructs comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms, in which the constructs have been selected for sequences that encode proteins that are involved in secondary metabolism. In some embodiments the donor organism is from an environmental sample, and the library is in a host cell.

Claim 3 of U.S. Patent No. 5,824,485 is drawn to a gene expression library comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms, in which the constructs have been selected for a specific property and the

constructs are operably linked to elements that allow for expression in a host cell. Claim 8 is drawn to the library of claim 3 in which the species of different organisms are derived from an environmental sample. Claim 10 is drawn to the library of claim 3 in which the constructs comprise metabolic pathway genes. Claims 21 and 22 of U.S. Patent No. 5,783,431 are not drawn to libraries selected for sequences that encode proteins that are involved in secondary metabolism.

Vining shows in the abstract that secondary metbolism genes are preferably isolated from genomes of different organisms because they are of ancient origin and are better conserved between species of organisms than within related genes of the same organism. Vining shows throughout many examples of secondary metabolism genes and that secondary metabolites are useful as antibiotics, mycotoxins, insecticides, and herbicides.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the library of claims 3, 8, and 10 of U.S. Patent No. 5,824,485 by selection for sequences that encode proteins involved in secondary metabolism because Vining shows that secondary metabolism genes are best obtained from different species of organisms and are useful to make antibiotics, mycotoxins, insecticides, and herbicides.

Conclusion

13. Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. For routine submissions the FAX number is (703) 308-4242. For FAX

transmissions in cases in which the Examiner has been notified by phone to expect the transmission, the FAX number is (703) 305-7939. In such cases please call the Examiner at (703) 308-4231 at the time of transmission to expedite delivery of the fax. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6 (d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca, Ph.D. whose telephone number is (703) 308-4231. The examiner can normally be reached on Monday through Friday from 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, Ph.D., can be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

John S. Brusca

John S. Brusca, Ph.D.

Patent Examiner

Application No.: 08/986181

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☑ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☑ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☑ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☑ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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